REMARKS

Claims 48-104 are all the claims pending in the application; claims 66-72 and 84-91 are rejected; claims 48-65, 73-83 and 92-104 have been withdrawn from consideration.

After entry of this Amendment, claims 48-65, 73-83 and 92-104 will be cancelled and claims 66-72 and 84-91 will be pending.

Support for the amendment to claim 66 to recite polypeptides comprising less than 566 amino acids of SEQ ID NO:2, and having bacteriophage polypeptide binding activity, may be found in Figure 10 and at page 105 of the specification. As shown therein, a polypeptide fragment of 565 amino acids was produced, and shown to have bacteriophage polypeptide binding activity.

Claim 70 has been amended to more clearly recite that which is being claimed. As the claim recites only those fragments and variants having 100% homology to the reference sequence, it only encompasses "fragments" (variants would contain amino acids other than those of the reference sequence). Therefore, reference to "variants" has been removed. Similarly, as only fragments are recited, the inclusion of the percentage of homology is redundant, and has thus also been removed.

Claim 72 has been amended to recite "*S. aureus* DnaG primase" in place of "STAAU_R9." As these two terms refer to the same polypeptide, no new matter has been added.

Support for the amendment to claims 84 and 91 (part (a)), can be found in the specification at page 58, line 36, through page 59, line 13, and page 29, line 24, through page 30, line 17.

Support for the amendment to claims 89 and 91 (part (b)), can be found in the specification at page 57, line 23, through page 58, line 3.

Support for the amendment to claims 90 and 91 (part (c)), can be found in the specification at page 57, line 23, through page 58, line 3.

Claim 91 has been amended to recite the biologically activities recited in claim 67.

No new matter has been added. Entry of the Amendment is respectfully requested.

I. Formal Matters

A. At paragraph 4 of the Office Action, the title is objected to as not being descriptive.

In response, Applicants include herewith an amendment to the title, such that the title is now more descriptive of the invention. In view of the amendment of the title, Applicants respectfully request reconsideration and withdrawal of this objection.

B. At paragraph 5 of the Office Action, the specification is objected due to the inclusion of a hyperlink.

In response, Applicants include herewith an amendment to the specification removing the hyperlink. In view of the amendment of the specification, Applicants respectfully request reconsideration and withdrawal of this objection.

II. Formal Matters

At paragraphs 6-7 of the Office Action, the claims are objected to for minor grammatical informalities and clarity.

In response, Applicants include herewith amendments to the claims addressing each of the issues raised by the Examiner. In view of the claim amendments, Applicants respectfully request reconsideration and withdrawal of these objections.

III. Rejection of Claims Under 35 U.S.C. §101

A. At paragraph 8 of the Office Action, claims 66-71 and 81-91 are rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The Examiner suggests removal of the term "enriched" to more clearly indicate the hand of man.

In response, Applicants include herewith amendments to the claims canceling the term as suggested by the Examiner. In view of the claim amendments, Applicants respectfully request reconsideration and withdrawal of this objection.

B. At paragraph 9 of the Office Action, claim 72 is rejected under 35 U.S.C. §101 as being directed to non-statutory subject matter. The Examiner suggests insertion of the term "purified" or "isolated" to indicate the hand of man.

In response, Applicants include herewith an amendment to claim 72 in the manner suggested by the Examiner. In view of the claim amendment, Applicants respectfully request reconsideration and withdrawal of this objection.

IV. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

A. At paragraph 11 of the Office Action, claims 66-71 and 81-91 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite due to the inclusion of the term "enriched."

In response, Applicants include herewith amendments to the claims canceling the term "enriched" as suggested by the Examiner. In view of the claim amendments, Applicants

respectfully assert that the claims are definite as written, and therefore request reconsideration and withdrawal of this objection.

B. At paragraph 12 of the Office Action, claim 91 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite due to the recitation of "biologically active." The Examiner states that scope of activities encompassed by the term is vague and unclear.

In response, Applicants include herewith an amendment to claim 91 to incorporate the subject matter of claim 67, and thereby define the specific functions of the claimed polypeptide, in place of the term "biologically active." In view of the claim amendment, Applicants respectfully assert that claim 91 is definite as written, and therefore request reconsideration and withdrawal of this objection.

V. Rejection of Claims Under 35 U.S.C. §112, First Paragraph

A. At paragraph 13 of the Office Action, claims 66-72, 84-87 and 89-91 are rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description support in the specification as filed.

The Examiner states that the rejected claims are drawn to a genus of bacterial polypeptide fragments, variants and domains, each with reference to the polypeptide of SEQ ID NO:2, that have the ability to bind a bacteriophage polypeptide or domain. The Examiner further states that genera of recited polypeptides is widely variant in both structure and function, and that only a single species of the genus is disclosed. The Examiner goes on to state that the single species fails to represent all species encompassed by the claimed genera, which encompasses a vast number of proteins, which are structurally and functionally diverse. The Examiner concludes

that given the lack of description of a representative number of species, the specification fails to describe the claimed invention in sufficient detail.

In response, Applicants respectfully traverse the Examiner's position for the following reasons.

First, in contrast to the Examiner's position, the present application describes more than a single species of the genus of polypeptides recited in the claims. As shown in Figure 10, at least thirteen different DnaG polypeptide fragments are described, of which at least seven have the bacteriophage polypeptide (96ORF78) binding activity recited in the claims. Therefore, Applicants submit that the current specification does provide "a representative number of species" for the claimed genus of polypeptides according to the requirements of MPEP § 2163 and according to the decision in *Eli Lilly* pointed out by the Examiner in the paragraph extending from page 5 to page 6 of the Office Action.

Second, the genus of polypeptides recited in the claims share a structural feature. As demonstrated in Figure 10, a "minimal domain" of 39 amino acids at the carboxyl terminus is required for the bacteriophage binding activity of the polypeptides encompassed by the claims.

Third, each member of the genus has the same functional feature, i.e., bacteriophage binding activity.

Applicants further assert that given the skill in the art and the disclosure in the specification, a person skilled in the art could easily make and obtain, without undue experimentation, variants of *S. aureus* DnaG having very minor sequence modifications and still having substantially the same ability to bind phage polypeptide(s) as the reference bacterial protein of SEQ ID NO:2. Indeed, given the knowledge of the 39 amino acid minimal domain,

the skilled artisan could clearly predict whether a particular fragment would fall within the scope of the claims. Similarly, as the preparation of variants by the addition, deletion or exchange of amino acids, or by the modification of the glycoside residues, is a trivial procedure well known in the art (see paragraph **B. (4)** hereinafter), those skilled in the art could easily identify additional DnaG polypeptide fragments or variants that bind to the bacteriophage polypeptide 96ORF78.

In conclusion, Applicants clearly provide a representative number of species of the claimed genus of polypeptides. Furthermore, each member of the claimed genus shares a common structural and functional feature. Therefore, Applicants respectfully assert that the specification does describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize that Applicants were in possession of the claimed invention, and request reconsideration and withdrawal of this rejection.

B. At paragraph 14 of the Office Action, claims 66-72, 84-87 and 89-91 are rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner states that while the specification is enabling for the isolated polypeptide of SEQ ID NO:2, it is not enabling for all bacterial polypeptide fragments or variants of SEQ ID NO:2, having the ability to bind a bacteriophage polypeptide. The Examiner concludes that undue experimentation would be required to make and/or use the entire scope of the claimed invention.

In response, Applicants respectfully traverse the Examiner's position for the following reasons.

As fully discussed above with regard to the written description rejection, Applicants assert that the specification provides a representative number of species of the claimed genus, and that the genus is well-defined in both structural and functional terms. Given the knowledge of the skilled artisan, and the disclosure in the specification, the skilled artisan would clearly be enabled to make and/or use the entire scope of the claimed invention without undue experimentation.

With respect to the *Wands* factors to be considered in determining whether undue experimentation is required, the following comments are provided in response to the Examiner's remarks.

(1) The breadth of the claims:

In contrast to the Examiner's position, Applicants respectfully assert that the claims are not overly broad. Indeed, claims 66 to 71 have been amended such that they are now restricted to those polypeptides comprising a fragment or variant of SEQ ID NO: 2 **having less than 566 amino acids**, and that **bind a bacteriophage polypeptide**. As currently recited in the claims, this genus of polypeptides does not encompass "any" or "all" polypeptides as suggested by the Examiner, but instead is **limited to a number of polypeptides clearly define by structure and activity**.

Similarly, claim 72 is restricted to polypeptide domains of **a specific origin** (derived from SEQ ID NO: 2 or derived from a bacteriophage polypeptide). The polypeptide domains encompassed by the claim must also posses a specific **physical property,** i.e. they must have the ability to **bind specifically to each other**.

Claims 84 to 91 have been amended to encompass polypeptides having a very high level of identity or similarity with a reference polypeptide.

Applicants again note that the disclosure is not limited to the isolated polypeptide of SEQ ID NO: 2 as suggested by the Examiner. The present application describes at least thirteen DnaG polypeptide fragments.

Applicants also respectfully refer the Examiner to *Utter v. Hiraga*, 6 USPQ2d 1709, 1714 (1988), wherein the court stated that "[a] specification may, within the meaning of 35 U.S.C. §112, first paragraph, contain a written description of a broadly claimed invention without describing all species that claim encompasses."

Applicants also submit that, as the Federal Circuit was satisfied in *Amgen Inc. v. Hoechst Marion Roussel Inc.* (F.3d Nos. 01-1191, 1218 (Fed. Cir. January 6, 2003)), any gaps between the instant disclosures and the claim breadth could be easily resolved by the skilled artisan without undue experimentation.

(2) The presence or absence of working examples:

The Examiner states at page 8, second paragraph, of the Office Action that "*The disclosure provides only a single working example of derivatives and mutants of SEQ ID NO: 2....This single working example....*" Applicants again respectfully note that, as shown in Figure 10, the present application describes at least thirteen DnaG polypeptide fragments, at least seven of which bind to a bacteriophage polypeptide (96ORF78). Thus, Applicants clearly provide more than a single working example of the "derivatives and mutants of SEQ ID NO:2."

The Examiner also states that the specification fails to provide guidance as to how to use those variant polypeptides "*having activities other than the desired activity, e.g. non-functional*

polypeptides or polypeptides having activity other that SEQ ID NO:2" (sentence bridging pages 8 and 9 of the Office Action). Applicants respectively point out that such polypeptides **are** either NOT covered by the claims (Claims 67 to 71 and 91) or explicitly mentioned to be useful: (i) in screening (p. 76-97), (ii) for raising antibodies especially useful for diagnostics, therapeutics and methods of drug screening and drug design (p.35, line 23) and (iii) as research reagents and materials for discovery of treatments of and diagnostics for diseases, particularly human diseases (p. 64 lines 26-29; p. 67-71).

Moreover, the Applicants refer the Examiner to the prior art references discussed in paragraph (4) hereinafter, teaching fully active mutants of DnaG primase.

(3) Predictability or unpredictability of the art:

As indicated herein before, the specification discloses a "minimal domain" of 39 amino acids (out of 599 amino acids) that is very important for binding of the bacteriophage polypeptide 96ORF78 by the *S. aureus* DnaG of the present application (see Figure 10). Knowing that critical information, those skilled in the art could easily identify additional DnaG polypeptide fragments or variants with the desired activity of binding a bacteriophage polypeptide, as recited in claims 66 to 72.

For those claims not limited to polypeptides with binding activity (Claims 84 to 91), Applicants note that the claimed bacterial polypeptides need express no activity to be used in the production of antibodies and/or for use in diagnostic methods.

Furthermore, the Courts have acknowledged that claims are not necessarily invalid if they encompass some inoperative embodiments (*see Atlas Powder Co. v. E. I. duPont de Nemours & Co.*, 750 F2d 1569, 224 USPQ 409 (Fed. Cir. 1984)).

If necessary, those skilled in the art could refer to the documents discussed hereinafter, disclosing relevant information about important domains for bacterial DnaG primase activity, or use in designing useful fragments and/or variants.

(4) The state of the prior art and relative skill of those in the art:

Applicants have reviewed the scientific documents referred to by the Examiner at pages 9-10 of the Office Action, and respectfully state that these documents are not relevant to the present invention.

The passage from Branden *et al.* cited by the Examiner refers to "*enzymes*" and to the design of "*de novo*" proteins. Clearly, based on the disclosure of the present application, there is no need for *de novo* design of polypeptides, nor any requirement for a specific enzymatic activity for polypeptides encompassed by the claims.

Witkowski *et al.* is also considered to be irrelevant because it concerns β-Ketoacyl synthases, which are very complex enzymes. Witkowski *et al.* indicates that β-Ketoacyl synthases "*consist of approximately 400 residues and typically form homodimers... β-Ketoacyl synthases constitute one of the catalytic domains of large molecular complexes, called multifunctional polypeptide...*" (p. 11643, 2nd column; emphasis added). Therefore, until proof to the contrary, Applicants submit that the unpredictability associated with alteration of a protein sequence is certainly much higher for complex "multifunctional" enzymes such as β-Ketoacyl synthases than it may be for the *S. aureus* DnaG primase of the present application.

As evidenced by the non-exhaustive list of scientific documents discussed hereinafter, the state of the art supports a relatively high level of predictability for domains important for bacterial DnaG primase activity.

(i) Ohnishi K. (Nucleic Acids Symp. Ser. (1985), 16:253-256) indicates that the C-terminal domain of the *E. coli* DNA primase is strongly homologous to the C terminal domain of the RPase beta subunit and to the RPase alpha, suggesting a common ancestor;

(ii) Tougu K. et al. (J. Biol. Chem. (1994) 269(6):4675-82) demonstrated that the N-terminal domain of 49 kDa from *E. coli* DNA primase is required for catalytic activity whereas the carboxy-terminal domain of 16 kDa is required for functional interaction with DnaB (helicase);

(iii) Sun et al. (PNAS (1994) 91:11462-66) have produced mutants of *E. coli* DNA primase lacking 10 and 40 C-terminal amino acids and having the same pRNA activity as wild-type primase;

(iv) Tougu and Marians (J. Biol. Chem. (1996) 271(35):21391-7) have produced a mutant *E. coli* DNA primase enzyme fully active as a primase;

(v) Sun and Godson (J. Mol. Biol. (1998) 276(4):689-703) have identified the DNA sequences required for binding *E. coli* primase;

(vi) Aravind L. et al. (Nucleic Acid Research (1998), 26(18):4205-13) have shown that type IA and II topoisomerases, OLD family nucleases, RecR proteins and DnaG-type primases all contain a common domain designated Toprim (topoisomerase-primase domain). This domain consists of approximately 100 amino acids and has two conserved motifs. Site-directed mutagenesis supports an important role for one of these two motifs in catalysis;

(vii) Pan H. et al. (Biochim. Biophys. Acta (1999), 1444(3):429-33) describe the cloning, expression and purification of *Bacillus stearothermophilus* DNA primase and crystallization of the zinc-binding domain;

(viii) Sun et al. (J. Bacteriol. (1999) 181(12):3761-7) demonstrated by mutagenesis only Lys241, and not Lys211 and Lys229, is part of the catalytic center of *E. coli* primase;

(ix) Keck et al. (Science (2000) 287(5462):2482-86) show a high resolution crystal structure of *E. coli* primase, including the catalytic core of the protein;

(x) Podobnik (J. Mol. Biol. (2000) 300(2):353-62) obtained the crystal structure of *E. coli* primase and showed that the Toprim domain of the protein is strikingly similar in its structure to that of corresponding domains in DNA topoisomerases;

(xi) Bird et al. (Biochemistry (2000) 39(1):171-82) have shown that the C-terminal domain of *Bacillus stearothermophilus* DNA primase interacts with DnaB (helicase) by making systematic truncations using limited proteolysis and PCR mutagenesis; and

Frick and Richardson (Annu. Rev. Biochem. (2001) 70:39-80) provide an extensive review of DNA primases functions and structure.

In view of the above, the Applicant submit that contrary to the Examiner's assertion, the prior art supports a low level of unpredictability and excellent expectation of success for obtaining DnaG fragments and mutants with desired DnaG primase activity.

(5) The amount of direction or guidance presented and the quantity of experimentation necessary:

As indicated hereinbefore, the specification provides both guidance AND working examples for fragments and variant polypeptides encompassed by the claims.

As also shown hereinbefore, there is not a high degree of unpredictability, as evidenced by the documents discussed in paragraph B. (4) above.

As pointed out in *In re Wands* (8 USPQ2d 1400, 1404) "*[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed*" (emphasis added). See also *In re Collianni* (561 F2d 220, 224, 195 USPQ 150, 153 (CCPA 1977)), the precursor of the Wands factors, wherein the Court said "*an extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance*" (emphasis added).

Accordingly, although it may be necessary to carry out further experimentation to assess the activity or functionality of some polypeptides encompassed by the claims, these experiments are within the abilities of the skilled artisan and do not require undue experimentation because the specification provides both guidance and working examples for the fragments and the variant polypeptides encompassed by the claims.

For all the above-mentioned reasons, the Applicants assert that the scope of the claims is not overly broad, and that based on the **evidence as a whole**, it is clear that those skilled in the art could practice the full scope of the claimed invention without undue experimentation.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

VI. Rejection of Claims Under 35 U.S.C. §102

A. At paragraph 15 of the Office Action, claims 66-71, 87 and 91 are rejected under 35 U.S.C. §102(b) as being anticipated by O'Donnell et al. (WO 99/37661, published July 29, 1999).

The Examiner states that claims 66-71 and 87 are drawn to polypeptide fragments or variants of SEQ ID NO:2, and optionally having the ability to bind a bacteriophage polypeptide. The Examiner further states that O'Donnell et al. teaches a polypeptide having primase activity encoded by *S. aureus dnaG* gene (pages 33-34), with 93.5% identity to SEQ ID NO:2, and 98.1% similarity to SEQ ID NO:2.

In response, Applicants note that claim 66 has been amended to encompass polypeptides comprising fragments and variants of the polypeptide set forth in SEQ ID NO:2, wherein the polypeptides comprises less than 566 amino acids of SEQ ID NO: 2. Furthermore, claim 66 and claims dependent therefrom recite an activity of the fragments and variants (binding a bacteriophage polypeptide).

In contrast, the polypeptide of O'Donnell comprises 572 amino acids. O'Donnell does not disclose specific examples of fragments of the polypeptide having less than 572 amino acids. Nor does O'Donnell teach or suggest which domain or how many amino acids of the polypeptide described therein is required for binding a bacteriophage polypeptide. Indeed, O'Donnell does not teach or suggest at all that the polypeptide described therein can bind a bacteriophage polypeptide.

While binding of a bacteriophage polypeptide may be an "intrinsic" property of the polypeptide disclosed by O'Donnell, polypeptides encompassed by the claims of the present application are not described in O'Donnell patent application. Accordingly, the polypeptide fragments and variants comprising less than 566 amino acids derived from SEQ ID NO: 2, and having the ability to bind a bacteriophage polypeptide, as recited in claims 66 to 71, are novel and not anticipated by O'Donnell.

As to claims 87 and 91, Applicants include herewith **Appendix I**, demonstrating that the polypeptide of SEQ ID NO:2 and the polypeptide of O'Donnell only share 92% similarity over the entire length of SEQ ID NO:2. As claims 87 and 91 (part (e)) recite a minimum of 95% similarity over the entire length of SEQ ID NO:2, the polypeptide of O'Donnell does not anticipate these claims.

In view of the comments above and the amendments to the claims, Applicants respectfully assert that the disclosure of O'Donnell does not teach each element of the claimed invention and therefore does not anticipate the rejected claims.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At paragraph 16 of the Office Action, claims 84 and 89-91 are rejected under 35 U.S.C. §102(e) as being anticipated by Doucette-Stamm et al. (USP 6,380,370).

The Examiner states that the rejected claims are drawn to polypeptide variants of SEQ ID NO:2, and that Doucette-Stamm teaches a polypeptide comprising an amino acid sequence that is at least 94% identical to amino acids 1-50 of SEQ ID NO:2, and comprises at least 10 contiguous amino acids of amino acids 1-34 of SEQ ID NO:2.

In response, Applicants include herewith an amendment to claims 84 and 91 (part (a)) such that the polypeptides recited therein have at least 92% identity with amino acids 1-34 of SEQ ID NO:2. As shown in the enclosed **Appendix II**, the corresponding region of the polypeptide of Doucette-Stamm has only 91% identity to amino acids 1-34 of SEQ ID NO:2. Therefore, Doucette-Stamm does not teach each element of claims 84 and 91, and does not anticipate these claims.

As to claims 89-91, these claims have been amended to recite at least 95% identity (claims 89 and 91 (part (b))) and at least 97% identity (claims 90 and 91 (part (c))) to amino acids 1-50 of SEQ ID NO:2. As noted by the Examiner, the corresponding region of the polypeptide of Doucette-Stamm has only 94% identity to amino acids 1-50 of SEQ ID NO:1 Therefore, Doucette-Stamm also does not teach each element of claims 89-91, and does not anticipate these claims.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

VII. Rejection of Claims Under 35 U.S.C. §103

At paragraph 17 of the Office Action, claims 66-71, 84-85, 87 and 89-91 are rejected under 35 U.S.C. §103(a) as being unpatentable over Benton et al. (USP 6,037,123), in view of Burgett et al. (USP 6,162,617) and Harbarth et al. (*Arch. Intern. Med.*, 1998).

The Examiner states that Benton et al. teaches a nucleic acid (SEQ ID NO: 34; clone pMP109) isolated from *S. aureus* encoding a polypeptide sharing 93.25% similarity to SEQ ID NO:2. As correctly pointed out by the Examiner, "Benton et al. do not teach a polypeptide encoded by their nucleic acid." Burgett et al. teaches cloning of the DnaG gene of *Streptococcus pneumoniae* and teaches expressing the novel protein encoded by the *dnaG* gene for use in screening for novel antibiotics. Harbarth et al. is merely referred to by the Examiner as a reference showing that *S. aureus* is known to cause bacterial infections in the human population.

The Examiner concludes that it would have been obvious to express the protein encoded by the polynucleotide of Benton, such action being motivated by the desire to determine if the encoded protein is a DNA primase as suggested by Benton, and to use the protein to screen for

novel antibiotics in view of the teachings of Burgett and Harbarth. The Examiner also concludes that the skilled artisan would have had a reasonable expectation of success for expressing the protein of Benton "because of the results of Benton et al."

In response, Applicants respectfully traverse the rejection for the following reasons.

A. First, Applicants submit that the Examiner has failed to carry his burden of establishing *prima facie* obviousness for claims 66 to 71. In order to establish obviousness, the Examiner must show the following: (1) there must be some suggestion or motivation, either in the cited references or in the knowledge generally available to one of ordinary skill in the art, to modify or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art must teach or suggest all claim limitations.

In rejecting the claims for obviousness, the Examiner disregarded the fact that claims 66 to 71 require that the claimed bacterial polypeptide fragment or variant "*binds a bacteriophage polypeptide.*" Thus, the Examiner did not include all claim limitations in the rejection.

At paragraph 18 of the Action, the Examiner does mention that binding a bacteriophage polypeptide "*is an inherent property of the polypeptide of O'Donnell et al. and Doucette-Stamm et al. and the polypeptide encoded by Benton et al.*" However, Applicants respectfully note, that which is inherent in the prior art cannot form a proper basis for rejecting the claimed invention as obvious under §103 (*see, e.g., In re Shetty*, 566 F2d 81, 195 USPQ 753 (CCPA 1977)). Quoting from *In re Spormann* (363 F2d 444, 448, 150 USPQ 449, 452 (CCPA 1966), the court said *"The inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown"* (*In re Shetty*, 566 F2d at 86, 195 USPQ at 757 (CCPA 1997)). (*See also In re Naylor*, 369 F2d

765, 768, 152 USPQ 106, 108 (CCPA 1966) ("*[Inherency] is quite immaterial if ... one of ordinary skill in the art would not appreciate or recognize the inherent result*"); *Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 1576, 230 USPQ 81, 88 (Fed. Cir. 1986), on remand sub nom., Crucible Inc. v. Stora Kopparbergs Bergslags AB, 701 F. Supp. 1157, 10 USPQ2d 1190 (W.D. Pa. 1988) (An inherent feature may be relied upon to establish obviousness only if the inherency would have been obvious to one of ordinary skill in the art: "Inherency and obviousness are distinct concepts.")*). Thus, the Examiner was legally incorrect in relying on inherency as a teaching or suggestion of an essential property of the claimed fragments or variants.

As the Examiner did not establish that the prior art teaches or suggests each of the claim limitations (i.e., the bacteriophage polypeptide binding ability of the claimed proteins), he did not established a *prima facie* case obviousness for claims 66 to 71.

B. Secondly, Applicants respectfully assert that none of the rejected claims are obvious in view of the cited references because the Examiner has not presented a clear and convincing motivation or suggestion for combining the cited references.

The Examiner's position is that claims 66-71, 84-85, 87 and 89-91, drawn to polypeptide variants of SEQ ID NO: 2, would have been obvious in view of the teaching of Benton et al. in combination with Burgett et al.

The following passage excerpted from the 1st par., page 14 of the Office Action, represents the core of the rejection. Therein the Examiner states that: "*one would have been motivated to express the protein encoded by the nucleic acid of Benton et al. in order to*

determine if the encoded protein is a DNA primase as suggested by Benton et al. ..." (emphasis added).

The Examiner further states that "*one would have a reasonable expectation of success for expressing the protein of Benton et al. because of the results of Benton et al.*" (emphasis added).

Applicants submit that, to the contrary, Benton et al. does not clearly suggest that the sequence disclosed therein encodes a DnaG primase. Indeed, in at least one respect, Benton teaches away from the polypeptides disclosed therein as primases. At column 89, Benton et al. emphasizes that "*Databases searches at both nucleic acid and peptide levels reveal identity at one end of the pMP109 clone* [the clone comprising the nucleotide sequence encoding the polypeptide sharing 93.25% similarity to SEQ ID NO:2] *to the plaC gene from S. aureus (Genbank Accession No. M63177) encoding a DNA-directed RNA polymerase (EC 2.7.7.6)*" (emphasis added). Thus, in this respect, Benton et al. suggests that the polypeptide disclosed therein may be a RNA polymerase, not a DNA primase.

Those skilled in the art wishing to express a DnaG primase protein in *S. aureus* would have been discouraged and not motivated to express the protein encoded by the nucleic acid sequence of Benton et al., in view of the teachings noted above.

Therefore, one skilled in the art would not have been motivated to express the protein encoded by the polynucleotide disclosed Benton et al., with the goal of obtaining *S. aureus* DnaG primase variants according to the present invention, in view of the noted teachings of Benton et al.

C. Third, Applicant submit that, contrary the Examiner's assertion, those skilled in the art would not have had a reasonable expectation of success of obtaining the polypeptides of

the invention "*because of the results of Benton et al.*" (excerpted from page 14 of the Office Action, 1st par.).

When discussing their results, Benton et al. emphasized that the sequence disclosed therein shares "identity" at both the nucleotide and peptide level to the *plaC* gene, but merely "similarity" to the DnaG polypeptide and only at the peptide level.

Moreover, as correctly pointed out by the Examiner, "*Benton et al. do not teach a polypeptide encoded by their nucleic acid.*" Neither Benton et al. nor Burgett et al. identify the correct open reading frame of the *S. aureus dnaG* polynucleotide. Accordingly, neither Benton et al. nor Burgett et al. give an indication or direction as to which of many possible choices is likely to be successful for expressing the *S. aureus* DnaG primase.

Therefore, one of ordinary skilled in the art would not have had a reasonable expectation of success of obtaining the claimed polypeptides by looking at the cited references, either alone or in combination.

Applicants submit that neither Benton et al. nor Burgett et al., alone or in combination, suggest the claimed invention. Even though the Examiner's impression may be that one skilled in the art might find it "obvious to try" to obtain the claimed invention, the Courts have repeated stated that "*whether a particular combination might be "obvious to try" is not a legitimate test for patentability*" (*In re Fine*, 5 USPQ 2d 1596, 1599; citations omitted)

Applicants conclude that the obviousness rejection of the cited claims is the result of an hindsight-based obviousness analysis of the prior art and thus Examiner has not established a *prima facie* case of obviousness for the rejected claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

VIII. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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